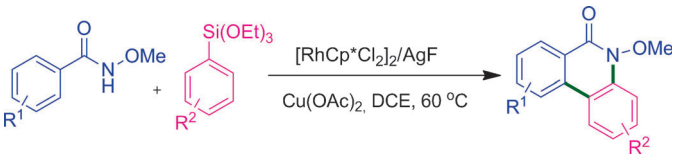
FULL PAPER



Keeping active: The rhodium-catalyzed C–H bond activation and annulation reactions of *N*-methoxybenzamides with aryltriethoxysilanes to give substituted phenanthridinone derivatives in good-to-excellent yields is described.

C–H Activation

*Natarajan Senthilkumar, Kanniyappan Parthasarathy, Parthasarathy Gandeepan, Chien-Hong Cheng** ____ ▮▮▮▮–▮▮▮▮

Synthesis of Phenanthridinones from *N*-Methoxybenzamides and Aryltriethoxysilanes through Rh^{III}-Catalyzed C–H and N–H Bond Activation

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Synthesis of Phenanthridinones from *N*-Methoxybenzamides and Aryltriethoxysilanes through Rh^{III}-Catalyzed C–H and N–H Bond Activation

Natarajan Senthilkumar, Kanniyappan Parthasarathy, Parthasarathy Gandeepan, and Chien-Hong Cheng*[a]

Abstract: An efficient method for the one-pot synthesis of substituted phenanthridinone derivatives from *N*-methoxybenzamides and aryltriethoxysilanes through rhodium-catalyzed dual C–H bond activation and annulation reactions is described. A double-cycle mechanism is proposed to account for this catalytic reaction. In addition, isotope-labeling studies were performed to understand the intimate mechanism of the reaction.

Keywords: annulation · C–H activation · phenanthridinones · rhodium · synthetic methods

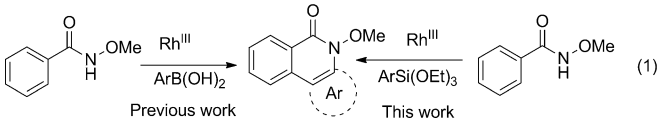
Introduction

In recent years, catalytic C–H bond activation by transition-metal complexes has become a powerful and attractive tool in organic synthesis.[1] In the C–H functionalization process, suitable heteroatoms in the substrates are commonly utilized to direct a metal complex towards a specific proximal C–H bond. Although many Pd-[2] and Rh^{I}-catalyzed transmetalation reactions[1a,3] that use arylsilanes as reagents have been reported, Rh^{III}-catalyzed transmetalation reactions of arylsiloxanes have rarely been explored.[4] The Hiyama coupling reaction of organosilanes with various aryl halides is well-known.[5] Recently, Shi and co-workers reported the direct oxidative arylation of substituted 2-phenyl pyridine by arylsilanes, which proceeded through a rhodium-catalyzed C–C bond cleavage.[4a] Miura and co-workers reported nickel-catalyzed C–H arylation and alkenylation reactions of heteroarenes with organosilicon reagents.[6] Arylsiloxanes are of particular interest because of their low toxicity and safe handling compared with other types of reagents.[7]

Wang et al. reported the synthesis of phenanthridinones by using *N*-methoxybenzamides with aryl iodides through Pd-catalyzed dual C–H activation reactions.[8] We have also developed a method for the synthesis of phenanthridinones from *N*-methoxybenzamides and arenes through multiple Pd-catalyzed C–H activation steps at room temperature.[9]

Several decades ago, this kind of benzannulation reaction towards the synthesis of phenanthrene from naphthylcarbene was reported by Dötz and co-workers.[10] The same group also reported the synthesis of a chromium-coordinated tetracyclic benzannulated product from a dibenzocycloheptenylidene complex.[11] Nakata and co-workers reported the total synthesis of kendomycin by using a Dötz intramolecular benzannulation reaction.[12]

Recently, a large number of rhodium-catalyzed C–H bond activation reactions that involve a benzannulation step have been developed, owing to their high catalytic activities, low catalyst loadings, and high regioselectivities.[13] In view of the advantage of using rhodium complexes as catalysts, we have examined and demonstrated the catalytic activity of rhodium(III) complexes for the oxidative coupling and annulation of *N*-methoxybenzamides with arylboronic acids to give phenanthridinone derivatives.[14] To date, there are no reports on the use of aryltrialkoxysilanes for the coupling and annulation reaction with *N*-methoxybenzamides through Rh^{III}-catalyzed C–H activation and annulation reactions. Our continuing interest in metal-catalyzed C–H activation[15] prompted us to explore the reaction of *N*-methoxybenzamides with aryltrialkoxysilanes. Herein, we report an effective method for the formation of phenanthridinone derivatives from *N*-methoxybenzamides and aryltrialkoxysilanes by using $[(RhCp^*Cl_2)_2]$ as the catalyst precursor [Eq. (1)].



(1)

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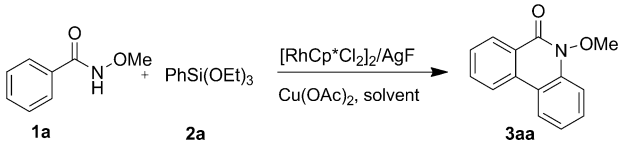
Results and Discussion

First, we chose *N*-methoxybenzamide (**1a**) and phenyltriethoxysilane (**2a**) as the substrates for the catalytic reaction. After testing a wide range of catalytic reactions conditions, we found that the treatment of compound **1a** (0.050 g, 0.33 mmol) with phenyltriethoxysilane (**2a**, 0.159 g, 0.66 mmol) in the presence of $[(RhCp^*Cl_2)_2]$ (0.0041 g, 2.0 mmol%), AgF (0.085 g, 0.66 mmol), and $Cu(OAc)_2$ (0.120 g, 0.66 mmol) in 1,2-dichloroethane (DCE, 2 mL) at 60 °C for 3 h gave phenanthridinone **3aa** in 82% yield. The structure of compound **3aa** was confirmed by its ^1H NMR, ^{13}C NMR, and mass spectra.

This rhodium-catalyzed C–H activation reaction appeared to greatly depend on the solvent, fluoride salt, and reaction temperature. First, we chose AgF/$Cu(OAc)_2$ as oxidants, based on literature reports, and tried to find a suitable solvent and reaction temperature. At high temperatures (130 °C and 100 °C), all of the solvents listed in Table 1 gave only trace amounts or no product formation. Next, we lowered the reaction temperature and tested the reaction with various solvents. At 60 °C, polar solvents, such as *tert*-amyl alcohol and EtOH, gave trace amounts of the product (Table 1, entries 1 and 2), but DMF and MeCN were completely inactive (Table 1, entries 3 and 4). Having failed to obtain product **3aa** by using polar solvents, various nonpolar solvents were employed. Among the solvents that we examined, DCE gave the highest yield of the phenanthridinone product (**3aa**) in 87% yield, as determined by integration of the NMR spectrum, or the isolated product in 82% yield (Table 1, entry 5). Other solvents, such as 1,2-dichlorobenzene (DCB), 1,4-dioxane, and toluene, were also effective, thus giving compound **3aa** in 20–55% yield (Table 1, entries 6–8), whereas THF failed to give compound **3aa** (Table 1, entry 9). The choice of fluoride source was also vital to the catalytic reaction. Of the fluoride sources that were tested, the best result was obtained with AgF, which afforded compound **3aa** in 82% yield (Table 1, entry 5). Other salts, like KF, CsF, and Bu_4NF, were less effective, thus giving compound **3aa** in low yields (Table 1, entries 10–12). In the absence of a copper salt, compound **3aa** was obtained in 42% yield (Table 1, entry 13). Next, the reaction was tested with 4.5 equivalents of the oxidant, instead of 4 equivalents. When the reaction was performed in the presence of 4.5 equivalents of AgF, compound **3aa** was formed in 91% yield (Table 1, entry 14). When 2 equivalents of AgF and 2.5 equivalents of $Cu(OAc)_2$ were used, the yield of compound **3aa** decreased slightly to 86% (Table 1, entry 15). When 1.0 equivalent of AgF and 3.5 equivalents of $Cu(OAc)_2$ were employed, the yield of compound **3aa** dramatically decreased (Table 1, entry 16). Longer reaction times (8 h and 12 h) did not have any effect on the yield of compound **3aa**. Without a Rh catalyst, the reaction failed to give compound **3aa** (Table 1, entry 17). When Ag_2O was used instead of AgF, no expected product was observed either (Table 1, entry 18).

Table 1. Optimization studies for the Rh^{III}-catalyzed synthesis of phenanthridinones from compounds **1a** and **2a**.[a]



1a 2a 3aa

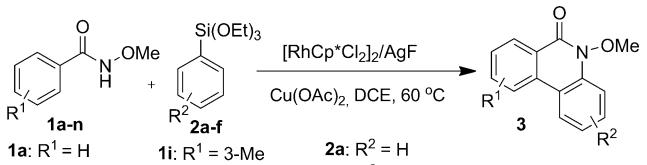
Entry	Fluoride salt	Solvent	Yield [%][b]
1	AgF	*t*-amylOH	<10
2	AgF	EtOH	<10
3	AgF	DMF	0
4	AgF	CH_3CN	0
5	AgF	DCE	87 (82)
6	AgF	DCB	55
7	AgF	toluene	20
8	AgF	1,4-dioxane	40
9	AgF	THF	0
10	KF	DCE	<10
11	CsF	DCE	20
12	Bu_4NF	DCE	15
13	AgF	DCE	42[c]
14	AgF	DCE	91[d]
15	AgF	DCE	86[e]
16	AgF	DCE	57[f]
17	AgF	DCE	0[g]
18	–	DCE	0[h]

[a] Unless otherwise noted, all of the reactions were performed by using *N*-methoxybenzamide (**1a**, 0.050 g, 0.33 mmol), arylsilane **2a** (0.159 g, 0.66 mmol), $[(RhCp^*Cl_2)_2]$ (4.1 mg, 0.0066 mmol), AgF (0.085 g, 0.66 mmol), and $Cu(OAc)_2$ (0.120 g, 0.66 mmol) in solvent (2 mL) at 60 °C for 3 h. [b] Yields were determined by integration of the ^1H NMR spectra. [c] AgF (0.66 mmol, 2.0 equiv) in the absence of $Cu(OAc)_2$. [d] AgF (4.5 equiv) in the absence of $Cu(OAc)_2$. [e] AgF (2 equiv) and $Cu(OAc)_2$ (2.5 equiv). [f] AgF (1 equiv) and $Cu(OAc)_2$ (3.5 equiv). [g] Without a Rh catalyst. [h] Ag_2O was used instead of AgF.

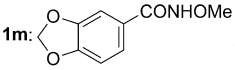
Under similar reaction conditions, various substituted *N*-methoxybenzamides (**1b**–**1n**) were reacted with compound **2a** to give their corresponding phenanthridinone derivatives (**3**, Table 2). Thus, 4-methylbenzamide (**1b**) afforded compound **3ba** in 87% yield. This catalytic reaction is nicely tolerant of halo substituents on the aromatic ring of the *N*-methoxybenzamides. As a result, 4-bromo-, 4-chloro-, and 4-fluoro-*N*-methoxybenzamides (**1c**–**1e**) afforded their corresponding phenanthridinones (**3ca**, **3da**, and **3ea**) in 84, 80, and 79% yield, respectively. This catalytic reaction also worked well with benzamides that contained electron-withdrawing CF_3 and NO_2 groups (**1f** and **1g**), thus giving phenanthridinones **3fa** and **3ga** in 75 and 78% yield, respectively. However, 4-cyano- and heteroaryl amides, such as benzofuran-2-amide and benzothiophene-2-amide, failed to give their corresponding phenanthridinones. The reaction of 4-phenyl-*N*-methoxybenzamide **1h** with compound **2a** provided phenanthridinone **3ha** in 81% yield. In all of these reactions, biphenyl was formed as a side product.

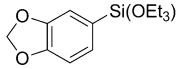
To understand the regioselectivity of *meta*-substituted *N*-methoxybenzamides in this catalytic reaction, we employed 3-methyl-, 3-bromo-, 3,4-dimethyl-, 3-nitro-, and 3,4-(methylenedioxy)-*N*-methoxybenzamides (**1i**–**1m**) as the substrates. For compounds **1i**–**1l**, their reactions with compound **2a** proceeded in a regioselective manner, in which C–H bond activation occurred at the less-hindered C6 posi-

Table 2. Rhodium-catalyzed annulation of *N*-methoxybenzamides with arylsilanes.[a]



1a: R^1 = H
1b: R^1 = 4-Me
1c: R^1 = 4-Br
1d: R^1 = 4-Cl
1e: R^1 = 4-F
1f: R^1 = 4-CF_3
1g: R^1 = 4-NO_2
1h: R^1 = 4-Ph
1i: R^1 = 3-Me
1j: R^1 = 3-Br
1k: R^1 = 3,4-diMe
1l: R^1 = 3-NO_2
1n: R^1 = 2-Cl
1o: R^1 = 4-CO_2Me
2a: R^2 = H
2b: R^2 = 4-Me
2c: R^2 = 4-OMe
2d: R^2 = 4-F
2e: R^2 = 3-Me
2f: R^2 = 3-OMe

1m: 

2g: 

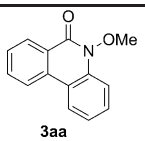
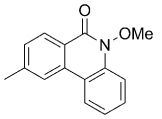
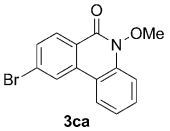
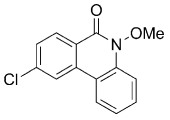
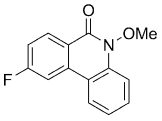
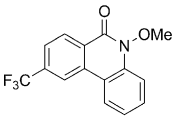
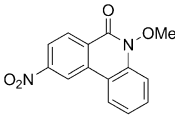
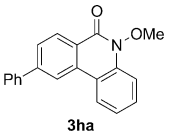
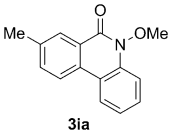
Entry	1	2	Product 3		Yield [%][b]
1	**1a**	**2a**		**3aa**	82
2	**1b**	**2a**		**3ba**	87
3	**1c**	**2a**		**3ca**	84
4	**1d**	**2a**		**3da**	80
5	**1e**	**2a**		**3ea**	79
6	**1f**	**2a**		**3fa**	75
7	**1g**	**2a**		**3ga**	78
8	**1h**	**2a**		**3ha**	81
9	**1i**	**2a**		**3ia**	80

Table 2. (Continued)

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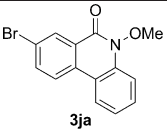
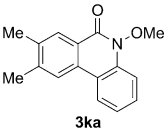
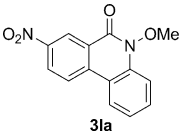
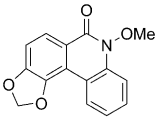
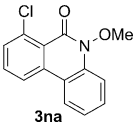
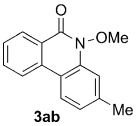
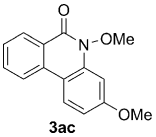
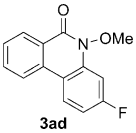
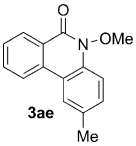
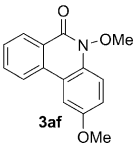
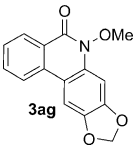
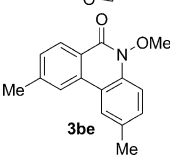
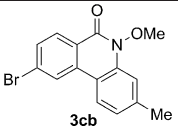
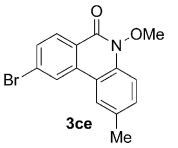
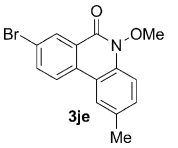
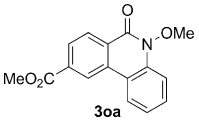
10	**1j**	**2a**		**3ja**	77
11	**1k**	**2a**		**3ka**	84
12	**1l**	**2a**		**3la**	70
13	**1m**	**2a**		**3ma**	74
14	**1n**	**2a**		**3na**	80
15	**1a**	**2b**		**3ab**	80
16	**1a**	**2c**		**3ac**	85
17	**1a**	**2d**		**3ad**	79
18	**1a**	**2e**		**3ae**	80
19	**1a**	**2f**		**3af**	75
20	**1a**	**2g**		**3ag**	87
21	**1b**	**2e**		**3be**	73

Table 2. (Continued)

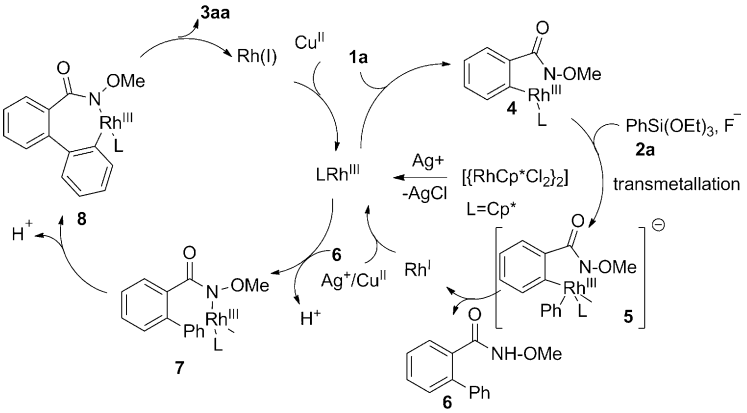
Entry	1	2	Product 3		Yield [%][b]
22	**1c**	**2b**		**3cb**	83
23	**1c**	**3e**		**3ce**	79
24	**1j**	**3e**		**3je**	81
25	**1o**	**2a**		**3oa**	69

[a] Unless otherwise noted, all of the reactions were performed by using substituted *N*-methoxybenzamide **1** (0.33 mmol), arylsilane **2** (0.66 mmol), $[(RhCp^*Cl_2)_2]$ (4.1 mg, 0.0066 mmol), AgF (0.085 g, 0.66 mmol), and $Cu(OAc)_2$ (0.120 g, 0.66 mmol) in DCE (2 mL) for 3 h. [b] Yield of isolated product.

tion to give products **3ia–la** in 70–84% yield. However, in the case of compound **1m**, contrary to the above observations, the activation occurred at the sterically hindered C2 position, instead of the less-hindered C6 position, to give compound **3ma** in 74% yield.[15f,16] In all of these cases, the other possible regioisomers were not observed. *ortho*-Chloro-substituted amide **1n** also reacted effectively with compound **2a** to give its corresponding phenanthridinone (**3na**) in 80% yield.

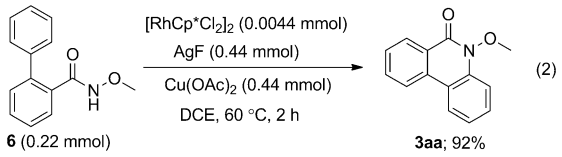
Having achieved the synthesis of phenanthridinones with various *N*-methoxybenzamide derivatives, we turned to the reaction of various aryltriethoxysilanes with compound **1a**. Thus, 4-methyl-, 4-methoxy-, and 4-fluorophenyltriethoxysilanes (**2b–2d**) with compound **1a** gave phenanthridinone derivatives **3ab**, **3ac**, and **3ad** in 85, 79, and 71% yield, respectively. To understand the regioselectivity of this reaction, 3-substituted phenyltriethoxysilanes were employed as the substrates in reactions with compound **1a**. Thus, 3-methyl- and 3-methoxyphenyltriethoxysilanes (**2e** and **2f**) provided compounds **3ae** and **3af** in 80 and 75% yield, respectively. No other regioisomeric products were detected in these reactions. However, in the case of 2-substituted siloxanes, such as 2-methyl- and 2-methoxyphenyltriethoxysilanes, the reactions failed to give their corresponding phenanthridinone derivatives. Then, we tested the reaction of compound **1a** with 3,4-(methylenedioxy)phenyltriethoxysilane. This reaction gave compound **3ag**, in which the C–N bond was formed at the less-hindered C6 position. Interestingly, this result is contrary to the C–H activation of 3,4-(methylenedioxy)-*N*-methoxybenzamide (**1m**), which occurred at the C2 position. Finally, the reactions of substituted *N*-methoxybenzamide derivatives **1b**, **1c**, and **1j** with substituted phenyltriethoxysilanes **2b** and **2e** also proceeded well. The expected reaction products (**3be**, **3cb**, **3ce**, and **3je**) were obtained in 73–83% yield.

Based on the chemistry of known rhodium-catalyzed C–H activation reactions, a possible mechanism that can account for this catalytic reaction is proposed in Scheme 1. The catalytic cycle is likely initiated by the removal of a chloride group from $[(RhCp^*Cl_2)_2]$ by a Ag^+ ion, followed by the deprotonated coordination of an amide nitrogen atom to the rhodium species and subsequent *ortho*-C–H activation to form a five-membered rhodacycle (**4**). Then, this intermediate undergoes a transmetalation reaction with a pentavalent silicate, which is generated in situ from the reaction of phenyltriethoxysilane (**2a**) with fluoride, to give a phenyl(benzamide)Rh^{III} species (**5**). Subsequent reductive elimination affords arylated *N*-methoxybenzamide (**6**) and a Rh^I species, which is oxidized into Rh^{III} by Ag^+ ions or $Cu(OAc)_2$. Deprotonation of the amide N–H group of compound **6**, followed by coordination to the Rh^{III} center, gives intermediate **7**. Further C–H activation at the *ortho*-carbon atom of the phenyl ring affords a seven-membered rhodacycle (**8**). Subsequent reductive elimination of compound **8**[18] gives the final product (**3aa**) and a Rh^I species, which is then converted into a Rh^{III} species by Cu^{II} or Ag^+ for the next catalytic cycle.

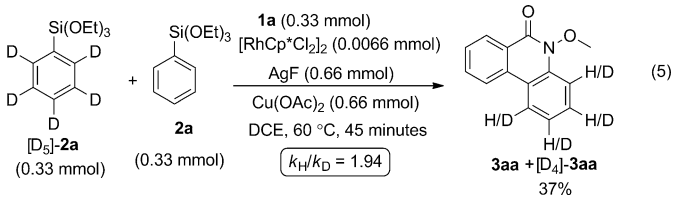


Scheme 1. Proposed mechanism for the formation of phenanthridinones.

To support the intermediacy of compound **6**, we prepared it independently by using a literature procedure.[8,9] The treatment of compound **6** under standard catalytic reaction conditions afforded compound **3aa** in 92% yield [Eq. (2)]. Notably, during the course of the catalytic reaction of compound **1a** with compound **2a** to give compound **3aa**, we could only observe the two substrates (**1a** and **2a**) and the final product (**3aa**), that is, we were unable to isolate or observe compound **6** (Scheme 1), thus suggesting that the further reaction of intermediate **6** to give the final product (**3aa**) is fast compared with the reaction between the two substrates (**1a** and **2a**).



(2)



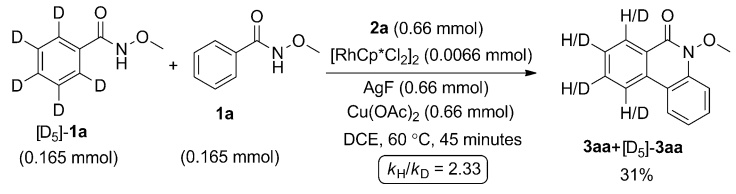
(5)

To further understand the intimate mechanism of this catalytic reaction, we measured the inter- and intramolecular kinetic isotope effects (KIEs) in the catalytic reaction of compound **1a** with compound **2a**. An intermolecular KIE of $k_H/k_D = 2.33$ was observed for the competition reaction between compound **1a** and deuterium-labeled [D_5]-**1a** with compound **2a** [Eq. (3)]. On the other hand, an intramolecular competition experiment between [D_1]-**1a** and compound **2a** gave a KIE of $k_H/k_D = 4.88$ [Eq. (4)]. The difference between these intermolecular and intramolecular KIE values indicates that the pre-binding of substrate **1a** (likely through the amide nitrogen atom) to the rhodium(III) center takes place prior to an irreversible C–H cleavage to form intermediate **4**. The substrate-binding step would not show selectivity for compound **1a** or [D_5]-**1a**. However, the subsequent C–H bond-cleavage step would give different rates. In general, a smaller KIE for the intermolecular competition reaction than the intramolecular competition reaction would be observed. The large primary KIE value (4.88) suggests that cleavage of the C–H bond would be the product-determining step and a primary KIE was observed.[17] We also performed an intermolecular competition reaction between phenyltriethoxysilanes [D_5]-**2a** and **2a** with compound **1a** to give products [D_4]-**3aa** or **3aa** [Eq. (5)]. We expect that there is no kinetic isotope effect for the *ortho*-phenylation of compound **1a** by compounds [D_5]-**2a** and **2a** to give intermediate **6** (Scheme 1), but the subsequent *ortho*-C–H bond cleavage of the phenyl ring should show an isotope effect. The measured KIE value is $k_H/k_D = 1.94$, in agreement with the fact that the binding of the phenyl ring of compound **6** to the rhodium center, which would not show selectivity for a C–H or C–D bond, presumably occurs before the C–H bond is cleaved.

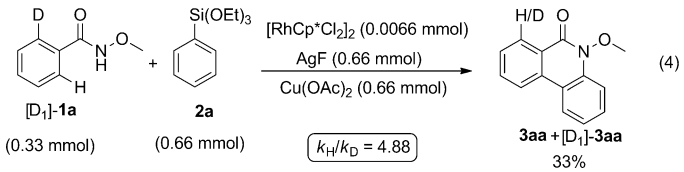
Interestingly, in this catalytic reaction, the aryl group in silane **2** acts like an aryne, by undergoing a [4+2] cyclization reaction with *N*-methoxybenzamide. Similar examples of the [4+2] cycloaddition of *N*-methoxybenzamide with an aryl iodide, arene, or arylboronic acid, catalyzed by palladium and rhodium complexes, are known. In addition, examples of [3+2] cycloaddition reactions of benzaldehyde oxime ether with an aryl iodide or an arylboronic acid, catalyzed by palladium complexes, have been reported.[15b,c,19] In all of these examples, the aryl group acts as an aryne equivalent by the removal of a proton on the *ortho*-carbon atom, presumably through C–H activation of the aryl group.

Conclusions

We have successfully developed a new method for the synthesis of substituted phenanthridinone derivatives in a highly regioselective manner from *N*-methoxybenzamides and aryltrialkoxysilanes through rhodium-catalyzed C–H bond activation and annulation reactions. The aryl group of the aryltrialkoxysilane acts like a benzyne equivalent by undergoing cyclization with *N*-methoxybenzamide to give the expected phenanthridinone product. Further application of this method in natural-product synthesis and investigation of the detailed reaction mechanism are underway.



(3)



(4)

Experimental Section

General Information

All of the reactions were performed under a nitrogen atmosphere on a dual-manifold Schlenk line, unless otherwise noted, in oven-dried glassware. All solvents were dried according to known methods and distilled prior to use.[20] All of the siloxanes were prepared from their corresponding aryl bromides according to a literature procedure.[21] ^{1}H NMR spectra were recorded at 400 MHz; ^{13}C NMR spectra were recorded at 100 MHz. Chemical shifts were calibrated to tetramethylsilane as an external standard.

General Procedure for the Synthesis of Phenanthridinones

A sealed tube that contained [$(RhCp^*Cl_2)_2$] (2.0 mol%), AgF (0.66 mmol), $Cu(OAc)_2$ (0.66 mmol), and amide **1** (0.33 mmol) was evacuated and purged with nitrogen gas three times. Then, DCE (2.0 mL) and siloxane **2** (0.66 mmol) were sequentially added to the system by syringe under a nitrogen atmosphere and the reaction mixture was stirred at 60 °C for 3 h. When the reaction was complete, the mixture was cooled and diluted with EtOAc (10 mL). The mixture was filtered through a pad of Celite and the Celite was washed with EtOAc (30 mL) and MeOH (20 mL). The combined filtrate was concentrated in vacuo and the residue was pu-

rified by column chromatography on silica gel (EtOAc/*n*-hexane, 1:10) to afford the desired product (**3**).

*7-Chloro-5-methoxyphenanthridin-6(5H)-one (**3na**)*

White solid; m.p. 150–152 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.54–8.53 (m, 1H), 8.27 (dd, J = 8.4 Hz, 3.4 Hz, 2H), 7.79–7.75 (m, 1H), 7.68–7.65 (m, 1H), 7.61–7.55 (m, 1H), 7.36–7.32 (m, 1H), 4.13 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.3, 135.8, 133.0, 132.6, 130.0, 128.5, 128.3, 128.1, 126.4, 123.2, 121.9, 118.6, 112.6, 62.7 ppm; IR (neat): $\tilde{\nu}$ = 1662, 1606, 1438, 1324 cm^{-1}; HRMS (FAB$^+$): m/z calcd for $C_{14}H_{10}ClNO_2$: 259.0400; found: 259.0402.

*3,5-Dimethoxyphenanthridin-6(5H)-one (**3ac**)*

White solid; m.p. 127–129 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.54 (d, J = 7.6 Hz, 1H), 8.19 (d, J = 8.0 Hz, 1H), 7.77–7.72 (m, 1H), 7.70 (st, J = 1.8 Hz, 1H), 7.60–7.56 (m, 2H), 7.23–7.14 (m, 1H), 4.11 (s, 3H), 3.92 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.7, 155.8, 145.4, 132.6, 132.4, 130.1, 128.4, 126.7, 121.9, 119.6, 117.1, 114.0, 107.0, 62.6, 55.8 ppm; IR (neat) $\tilde{\nu}$ = 1645, 1519, 1437 cm^{-1}; HRMS (FAB$^+$): m/z calcd for $C_{15}H_{13}NO_3$: 255.0895; found: 255.0895.

*3-Fluoro-5-methoxyphenanthridin-6(5H)-one (**3ad**)*

White solid; m.p. 182–184 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.56–8.52 (m, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.86–7.83 (m, 1H), 7.66–7.57 (m, 2H), 7.35–7.24 (m, 2H), 4.11 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.6 (d, J(C,F) = 251.5 Hz), 156.6, 136.2, 135.5 (d, J(C,F) = 9.1 Hz), 131.6 (d, J(C,F) = 9.8 Hz), 130.7, 123.4, 123.3, 122.8, 117.7 (d, J(C,F) = 3.8 Hz), 116.3 (d, J(C,F) = 23.5 Hz), 112.7, 107.9 (d, J(C,F) = 23.5 Hz), 62.7 ppm; IR (neat) $\tilde{\nu}$ = 2071, 1635, 1310 cm^{-1}; HRMS (FAB$^+$): m/z calcd for $C_{14}H_{10}FNO_2$: 243.0696; found: 243.0691.

*5-Methoxy-4-methylphenanthridin-6(5H)-one (**3ae**)*

White solid; m.p. 189–191 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.52 (d, J = 8.0 Hz, 1H), 8.22 (d, J = 8.0 Hz, 1H), 8.13 (d, J = 8.0 Hz, 1H), 7.76–7.72 (m, 1H), 7.57–7.53 (m, 1H), 7.47 (s, 1H), 7.16–7.14 (m, 1H), 4.13 (s, 3H), 2.52 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.4, 140.6, 135.8, 133.1, 132.5, 128.5, 127.6, 124.4, 123.1, 121.7, 116.2, 112.7, 62.7, 21.9 ppm; IR (neat) $\tilde{\nu}$ = 2952, 1670, 1492 cm^{-1}; HRMS (FAB$^+$): m/z calcd for $C_{15}H_{13}NO_2$: 239.0946; found: 239.0945.

*6-Methoxy-[1,3]dioxolo[4,5-b]phenanthridin-5(6H)-one (**3ag**)*

White solid; m.p. 203–205 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.49–8.47 (m, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.72–7.68 (m, 1H), 7.58 (s, 1H), 7.52–7.48 (m, 1H), 7.14 (s, 1H), 6.06 (s, 2H), 4.09 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.1, 150.0, 144.6, 133.0, 132.5, 132.1, 128.5, 127.0, 125.2, 121.4, 112.3, 101.9, 93.9, 62.6 ppm; IR (neat) $\tilde{\nu}$ = 2340, 1657, 1614 cm^{-1}; HRMS (FAB$^+$): m/z calcd for $C_{15}H_{11}NO_4$: 269.0688; found: 269.0685.

*5-Methoxy-2,9-dimethylphenanthridin-6(5H)-one (**3be**)*

White solid; m.p. 150–152 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.40 (d, J = 8.0 Hz, 1H), 8.01 (s, 2H), 7.52 (d, J = 8.4 Hz, 1H), 7.36 (t, J = 7.5 Hz, 2H), 4.09 (s, 3H), 2.53 (s, 3H), 2.47 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.1, 143.0, 133.8, 132.8, 132.5, 130.8, 129.3, 128.4, 124.1, 123.2, 121.9, 118.4, 112.5, 62.6, 22.1, 21.1 ppm; IR (neat) $\tilde{\nu}$ = 2935, 1666, 1620 cm^{-1}; HRMS (FAB$^+$): m/z calcd for $C_{16}H_{15}NO_2$: 253.1103; found: 253.1101.

*9-Bromo-5-methoxy-3-methylphenanthridin-6(5H)-one (**3cb**)*

Brown solid; m.p. 210–212 °C; ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 8.36 (d, J = 8.8 Hz, 1H), 8.33 (s, 1H), 8.04 (d, J = 8.0 Hz, 1H), 7.64 (t, J = 8.4 Hz, 1H), 7.45 (s, 1H), 7.15 (t, J = 8.0 Hz, 1H), 4.11 (s, 3H), 2.51 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.9, 141.5, 136.2, 134.7, 130.8, 130.3, 128.0, 124.7, 124.6, 124.5, 123.2, 114.9, 112.8, 62.7, 21.9 ppm; IR (neat) $\tilde{\nu}$ = 1670, 1599, 1475 cm^{-1}; HRMS (FAB$^+$): m/z calcd for $C_{15}H_{12}BrNO_2$: 317.0051; found: 317.0050.

*9-Bromo-5-methoxy-2-methylphenanthridin-6(5H)-one (**3ce**)*

Brown solid; m.p. 194–196 °C; ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 8.38–8.36 (m, 2H), 7.94 (s, 1H), 7.66 (dd, J = 8.4 Hz, 1H), 7.53 (d, J = 8.4 Hz, 1H), 7.41–7.39 (m, 1H), 4.09 (s, 3H), 2.47 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.9, 141.5, 136.2, 134.7, 130.8, 130.3, 128.0, 124.7, 124.6, 124.5, 123.2, 114.9, 112.8, 62.7, 21.9 ppm; IR (neat) $\tilde{\nu}$ = 1669, 1599, 1475 cm^{-1}; HRMS (FAB$^+$): m/z calcd for $C_{15}H_{12}BrNO_2$: 317.0051; found: 317.0045.

*8-Bromo-5-methoxy-3-methylphenanthridin-6(5H)-one (**3je**)*

White solid; m.p. 202–204 °C; ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 8.65 (sd, J = 2.4 Hz, 1H), 8.09 (d, J = 8.4 Hz, 1H), 7.96 (s, 1H), 7.82 (dd, J = 9.0 Hz, 2.2 Hz, 1H), 7.53 (d, J = 8.4 Hz, 1H), 7.41–7.38 (m, 1H), 4.09 (s, 3H), 2.47 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.9, 135.5, 133.6, 133.1, 131.7, 131.4, 131.1, 127.8, 123.7, 123.2, 122.0, 117.7, 112.7, 62.7, 21.1 ppm; IR (neat) $\tilde{\nu}$ = 1669, 1599, 1478 cm^{-1}; HRMS (FAB$^+$): m/z calcd for $C_{15}H_{12}BrNO_2$: 317.0051; found: 317.0054.

Intermolecular Kinetic Isotope Effect [Eq. (3)]

A sealed tube that contained [(RhCp*Cl$_2$)$_2$] (2.0 mol%), AgF (0.66 mmol), Cu(OAc)$_2$ (0.66 mmol), and a mixture of amides **1a** (0.165 mmol) and [D$_5$]-**1a** (0.165 mmol) was evacuated and purged with nitrogen gas three times. Then, DCE (2.0 mL) and phenyltriethoxysilane (**2a**, 0.66 mmol) were sequentially added to the system by syringe under a nitrogen atmosphere and the reaction mixture was stirred at 60 °C for 45 min. Then, the mixture was cooled and diluted with EtOAc (10 mL). The mixture was filtered through a pad of Celite and the Celite was washed with EtOAc (30 mL) and MeOH (20 mL). The combined filtrate was concentrated in vacuo and the residue was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 1:10) to afford the desired products (**3aa** and [D$_5$]-**3aa**) in a combined 31% yield. ^{1}H NMR analysis of the mixture gave k_H/k_D = 2.33.

Intramolecular Kinetic Isotope Effect [Eq. (4)]

A sealed tube that contained [(RhCp*Cl$_2$)$_2$] (0.0066 mmol), AgF (0.44 mmol), Cu(OAc)$_2$ (0.44 mmol), and amide [D$_1$]-**1a** (0.33 mmol) was evacuated and purged with nitrogen gas three times. Then, DCE (2.0 mL) and phenyltriethoxysilane (**2a**, 0.66 mmol) were sequentially added to the system by syringe under a nitrogen atmosphere and the reaction mixture was stirred at 60 °C for 45 min. Then, the mixture was cooled and diluted with EtOAc (10 mL). The mixture was filtered through a pad of Celite and the Celite was washed with EtOAc (30 mL) and MeOH (20 mL). The combined filtrate was concentrated in vacuo and the residue was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 1:10) to afford the desired products (**3aa** and [D$_1$]-**3aa**) in a combined 33% yield. ^{1}H NMR analysis of the mixture gave k_H/k_D = 4.88.

Intermolecular Kinetic Isotopic Effect [Eq. (5)]

A sealed tube that contained [(RhCp*Cl$_2$)$_2$] (0.0066 mmol), AgF (0.66 mmol), Cu(OAc)$_2$ (0.66 mmol), and *N*-methoxybenzamide (**1a**, 0.33 mmol) was evacuated and purged with nitrogen gas three times. Then, DCE (2.0 mL) and mixture of phenyltriethoxysilane (**2a**, 0.33 mmol) and [D$_5$]-**2a** (0.33 mmol) were sequentially added to the system by syringe under a nitrogen atmosphere and the reaction mixture was stirred at 60 °C for 45 min. Then, the mixture was cooled and diluted with EtOAc (10 mL). The mixture was filtered through a pad of Celite and the Celite was washed with EtOAc (30 mL) and MeOH (20 mL). The combined filtrate was concentrated in vacuo and the residue was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 1:10) to afford the desired products (**3aa** and [D$_1$]-**3aa**) in a combined 37% yield. ^{1}H NMR analysis of the mixture gave k_H/k_D = 1.94.

Cyclization of ortho-Arylated N-Methoxybenzamides [Eq. (2)]

A sealed tube that contained [(RhCp*Cl$_2$)$_2$] (0.0044 mmol), AgF (0.44 mmol), Cu(OAc)$_2$ (0.44 mmol), and *N*-methoxy-[1,1′-biphenyl]-2-carboxamide (**6**, 0.22 mmol) was evacuated and purged with nitrogen gas

three times. Then, DCE (2.0 mL) was added to the system by syringe under a nitrogen atmosphere and the reaction mixture was stirred at 60 °C for 2 h. Then, the mixture was cooled and diluted with EtOAc (10 mL). The mixture was filtered through a pad of Celite and the Celite was washed with EtOAc (30 mL) and MeOH (20 mL). The combined filtrate was concentrated in vacuo and the residue was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 1:10) to afford the desired product (**3aa**) in 92 % yield.

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